REMARKS

Telephonic inquiry

Applicants thank the Examiner for the telephonic inquiry of October 28, 2009. This paper is being filed in response thereto. The amendments presented in the Reply filed July 20, 2009 have been entered.

Claims

Claims 1–19 are pending, of which, claims 1–5, 9–10, 18 and 19 have been elected for prosecution herein pursuant to the restriction requirement of June 25, 2007.

Claims 6–8 and 11–17 are withdrawn from consideration pursuant to the forgoing restriction/election.

Claims 20 and 21 are cancelled without prejudice or disclaimer.

Claim 23 is added by this paper.

Applicants gratefully acknowledge the allowability of claims 18 and 19.

Claim amendments

Claim 1 has been amended to incorporate the 95% sequence identity aspect, as per the Examiner's suggestion. Applicants' amendment of the claim is not be construed with acquiescence to any ground of rejection.

Amended claim 1 and new claim 22 are supported by the disclosure contained in, for example, paragraph [0020] (e.g., "nucleotide sequence of SEQ ID NO: 1"), paragraph [0025] (e.g., "sufficient homology") and paragraph [0032] (e.g., "at least 80% homology, preferably 90% homology") of the published application. Applicants further submit that in view of the replete information available to the skilled worker regarding methods/tools for calculating homology, the structural information (e.g., polynucleotide sequence) of molecules having 80% or 90% or 95% homology to a given polynucleotide sequence of SEQ ID NO: 1 can at once be envisaged. Thus the specification literally discloses 80% –100% and 90% –100% homology.

Claim 1 further recites the elements of claim 21, which is hereby cancelled without prejudice or disclaimer. Claims 4, 5, 9 and 10 have been amended as per the Examiner's suggestion.

Applicants submit that the claim amendments do not raise new matter. Furthermore, insofar as the structural (e.g., sequence homology) and functional (e.g., binding to PKA regulatory subunit II) features recited in the claims have been previously examined, the claim amendments do not impose additional search burden. See, MPEP §714.13. Entry thereof is

earnestly solicited.

Sequence Listing

The Examiner is thanked for her careful review of the sequence listing. SEQ ID NO: 1 and SEQ ID NO: 2 are now identified as belonging to rat (*Rattus norvegicus*) sequences. Support for the correction of this obvious typographical error can be found, at least, in the Examples. See for example, the description of FIG. 7 in paragraph [0096] of the published application, wherein it is taught that "AQP2, PKA and AKAP18δ and/or a 55 kDa AKAP are present on the same intracellular vesicles. The inner medulla of rat kidneys was homogenized, and the nuclei and cell debris were removed by centrifugation. The resulting post-nuclear supernatant was incubated with affinity-purified anti-AKAP18δ antibodies coupled to an Eupergit ClZ methacrylate matrix (AKAP18AB beads)." FIG 10 further describes the localization of AKAP18δ along with other interacting proteins in rat heart cells. Moreover, inasmuch as information on the nature of the recited sequences was readily available to the skilled worker via GenBank or EBI databases (see, page 2, last paragraph of the Office Action), Applicants respectfully submit that the correction thereof to recite the rodent origin of SEQ ID NOs: 1 and 2 does not raise new matter.

Entry thereof is earnestly solicited.

Rejection under 35 U.S.C. §112, ¶1 (written description)

While applicants may not agree with the agency's interpretation of the elements necessary to meet the statutory requirements of 35 U.S.C. § 112, ¶1, nonetheless, the pending claims have been amended to substantially conform to these.

One aspect of Applicants' invention, which is claimed herein, is directed to polynucleotide sequences comprising at least 95% homology to SEQ ID NO: 1 and which encode proteins having PKA-regulatory subunit II-binding activity. It is submitted that present claim 1 conforms to exemplary claims 1 and 2 of Example 11B beginning on Page 39 of the *Training Materials* (Rev. 1, March 25, 2008) of the PTO's new *Written Description Guidelines*.

The PTO's contention that the disclosure of specific examples of AKAPδ polynucleotide sequences, i.e., SEQ ID NO: 1, fails to provide adequate written description for the genus of the claimed polypeptides is respectfully traversed. Firstly, this is different from *University of California v. Lilly, 964 F.2d 1128 (Fed.Cir. 1997)* or *University of Rochester v. Searle, 358 F.3d 1303 (Fed.Cir. 2004)* where functional language was involved with insufficient structural details available for a chemical compound. These facts here are similar to those in *Capon v. Eshhar*, 76 USPQ2d 1078, 1082 (Fed. Cir. 2005) and *Falkner v. Inglis,* 448 F.3d 1357 (Fed.Cir. 2006). In these cases, the

court held that even where there are no examples within the scope of a claimed genus, a written description exists where the elements of the members of the genus are known. Here, based on the complete disclosed AKAPδ polynucleotide sequence (i.e., SEQ ID NO: 1), variant sequences are *also* comprehensible without explicitly listing each and every sequence. The specification provides representative examples of polynucleotide sequences which fall within this genus of polynucleotides, for example, SEQ ID NO: 1 and degenerates thereof. Furthermore, in view of the detailed level of knowledge in molecular biology and the sophisticated tools available to the skilled worker, *any* variant sequence which meets the claimed structural (i.e., nucleotide sequence) can be can be generated. For example, the sequences can be generated using Lasergene Software available via DNAstar Inc. Additionally, functional features (e.g., PKA regulatory subunit II-binding ability, as taught by the present specification) of these variants can be routinely tested, for example, using assays that are described in the present specification. Explicit description is therefore not necessary.

It is therefore courteously submitted that Applicants' claims 1–5, 9–10, 18 and 19, in the current form, fully comply with the statutory requirements of 35 U.S.C. §112, ¶1 with respect to written description. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §112, ¶1 (enablement)

With respect to variant sequences, the Examiner alleges that the genus of polynucleotides is "very large." The Examiner alleges that at 80% identity, the number of variants is roughly 3 x 10^{23}. The Examiner at page 6 proceeds to allege that "it would take undue experimentation to make the variants of the polypeptide set forth by SEQ ID NO: 2 and test all the variant polypeptides for binding to any structure having PKA regulator subunit II." As such, instant claim 20, which recites the functional language, is also rejected under this section. The corroborating evidence provided by Hundrucker et al. (2006) was not considered since it was post-published. Additionally, the disclosure in Schneider et al. (1998) was not taken into consideration because "the reference only discloses design of variant peptides of 10 amino acids." See, page 5 of the Office Action.

Reconsideration of this rejection, in view of the foregoing amendments, further in view of the precedential opinion issued by the United States Board of Patent Appeals and Interferences (*Ex parte* Kubin, Appeal No. 2007-0819, B.A.P.I. 2007) is earnestly solicited. The genus of the molecules claimed herein is small enough that the skilled artisan can output each and every sequence using routine computational methods. Moreover, insofar as the structural determinants of the variant sequences are expressed in terms of homology, the skilled worker

can use routine techniques, such as homology mapping, to further identify candidate nucleotides which meet the structural aspects recited in the claims. Conserved amino acid substitutions (see *infra* for a discussion thereof) could be used as high-stringency filters. Additionally, as is routinely conducted in bioinformatics, variant sequences having an abrupt stop codon, no start codon, etc. can be removed from this pool. As for the functional aspect recited in the claims, the skilled worker could use high throughput screening of variant sequences, for example, using FRET studies described in Applicants' own specification. Other high-throughput techniques for studying protein-protein interactions, for example, mammalian-2-hybrid or yeast-2-hybrid screens, may also be utilized. Reagents and methodologies used in such assays were known to the skilled worker before the earliest priority date.

In view of the aforementioned amendments and remarks, it is respectfully submitted that Applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention with an effort that is routine with in the art. Withdrawal of the rejection under 35 U.S.C. §112, ¶1, is respectfully requested.

Rejection under 35 U.S.C. §112, ¶2

Claims 4, 5, 9 and 10 have been amended as per the Examiner's suggestion, rendering the rejection thereof under this section moot.

The Office Action alleges that the claimed variants are non-enabled because the term "conserved substitution" is vague and indefinite. Applicants submit that based solely on this contention, the rejection rests on the issue of claim definiteness (i.e., §112, ¶2) and not on enablement. Correction thereof is earnestly requested.

In the reply filed December 30, 2009, Applicants demonstrated that the art is replete with information on degeneracy of the genetic code, conserved amino acid substitutions, replacement of analogous amino acid residues with structurally similar amino acids, and the like. Moreover, the disclosure in WO 99/62933 or WO 02/38592, which were available to the skilled worker before the earliest filing date of the instant application, provide detailed guidance of such amino acid substitutions.

In response the PTO contends that "the specification fails to disclose the list of examples [of conserved substitutions] and fails to disclose the teachings of WO 99/62933 and WO 02/38592." See page 5, ¶1 of the Office Action. This contention and the rejection based thereon are both respectfully traversed.

It is by now well-settled that a term that is not used or defined in the specification is not indefinite if the meaning of the claim term is discernible. *Bancorp Services, L.L.C. v. Hartford Life*

Ins. Co., 359 F.3d 1367, 1372, 69 USPQ2d 1996, 1999-2000 (Fed. Cir. 2004). Such is clearly the case here. Moreover, as explicitly stated under §2173.02 of the MPEP "The requirement to 'distinctly' claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles. Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite." See also *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1366, 71 USPQ2d 1081, 1089 (Fed. Cir. 2004). A simple search on PUBMED can verify that, contrary to the Examiner's contention, conserved amino acid substitution was understood in the art well before the filing date of the instant application. For example, five scientific publications, all of which were published before the earliest priority date of September 6, 2002, contain the exact search phrase "conserved amino acid substitution" in the Title or Abstract. As an example, the Examiner is requested to review the enclosed article by Wu et al. (*Proc Int Conf Intell Syst Mol Biol.*, 4:230-40, 1996). Accordingly, in view of the aforementioned arguments and references, further in line with the decision in *Capon v. Eshhar v. Dudas* (see *supra*), the Examiner is requested to withdraw this rejection.

If there are any remaining issues which can be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

No fees are believed to be due with this paper; however, the Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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